

SEQUENCE LISTING



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<120> Production of Antibodies

<130> PNK/060113/0275850 - T7060C

<140> US 09/737,476

<141> 2000-12-18

<150> EP 99310188.0

<151> 1999-12-17

<160> 67

<170> MS Word

<210> 1

<211> 440

<212> DNA

<213> Artificial Sequence

<220>

<223> VHH with peptide linker

<220>

<221> CDS

<222> (1)..(417)

<400> 1

cag gtg cag ctg cag gag tca ggg gga gga ttg gtg cag gct ggg ggc 48
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15

tct ctg aga ctc tcc tgt gca gcc tcg gga cgc gcc acc agt ggt cat 96
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser Gly His
20 25 30

ggt cac tat ggt atg ggc tgg ttc cgc cag gtt cca ggg aag gag cgt 144
Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys Glu Arg
35 40 45

gag ttt gtc gca gct att agg tgg agt ggt aaa gag aca tgg tat aaa 192
Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp Tyr Lys
50 55 60

gac tcc gtg aag ggc cga ttc acc atc tcc aga gat aac gcc aag act	240
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr	
65 70 75 80	
acg gtt tat ctg caa atg aac agc ctg aaa cct gaa gat acg gcc gtt	288
Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val	
85 90 95	
tat tat tgt gcc gct cga ccg gtc cgc gtg gat gat att tcc ctg ccg	336
Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser Leu Pro	
100 105 110	
gtt ggg ttt gac tac tgg ggc cag ggg acc cag gtc acc gtc tcc tca	384
Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser	
115 120 125	
gaa caa aaa ctc atc tca gaa gag gat ctg aat taataagggc taagctcgaa	437
Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn	
130 135	
ttc	440

<210> 2

<211> 139

<212> PRT

<213> Artificial Sequence

<220>

<223> VHH with peptide linker

<400> 2

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly	
1 5 10 15	
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser Gly His	
20 25 30	
Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys Glu Arg	
35 40 45	
Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp Tyr Lys	
50 55 60	
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Thr	
65 70 75 80	
Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val	
85 90 95	
Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser Leu Pro	
100 105 110	
Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser Ser	
115 120 125	

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn
130 135

<210> 3

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> myc linker

<400> 3

Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu Asn
1 5 10

<210> 4

<211> 471

<212> DNA

<213> Artificial Sequence

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (1)..(459)

<400> 4

cag gtg cag ctg cag cag tca ggg gga ggc ttg gtg cag gct ggg ggg 48
Gln Val Gln Leu Gln Gln Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15

tct ctg aga ctc tcc tgt gta gct tct gaa agc agc ttc agc aac aat 96
Ser Leu Arg Leu Ser Cys Val Ala Ser Glu Ser Ser Phe Ser Asn Asn
20 25 30

cac atg ggc tgg tac cgc cgg gct cca ggg aac cag cgc gag ctg gtc 144
His Met Gly Trp Tyr Arg Arg Ala Pro Gly Asn Gln Arg Glu Leu Val
35 40 45

gca act att agt cct ggt ggt agc aca cac tat gta gac tcc gtg aag 192
Ala Thr Ile Ser Pro Gly Gly Ser Thr His Tyr Val Asp Ser Val Lys
50 55 60

ggc cga ttc acc atc tcc cga gac aac gcc aag aac aca gtg tat cta Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu 65 70 75 80	240
caa atg gac agc ctg aaa cca gag gac acg gcc gtc tat tac tgt gct Gln Met Asp Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95	288
gcc aag ggg agg ggg ctg cag gct atg cag tac tgg gcc cag ggg acc Ala Lys Gly Arg Gly Leu Gln Ala Met Gln Tyr Trp Gly Gln Gly Thr 100 105 110	336
ctg gtc acc gtc tcc tca gcg cac cac agc gaa gac ccc agc tcc gcg Leu Val Thr Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ser Ala 115 120 125	384
gcc gcc cat cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc Ala Ala His His His His His His Gly Ala Ala Glu Gln Lys Leu Ile 130 135 140	432
tca gaa gag gat ctg aat ggg gcc gca tagtaacaat tg Ser Glu Glu Asp Leu Asn Gly Ala Ala 145 150	471
<210> 5	
<211> 153	
<212> PRT	
<213> Artificial Sequence	
<220>	
<223> VHH with linker	
<400> 5	
Gln Val Gln Leu Gln Gln Ser Gly Gly Gly Leu Val Gln Ala Gly Gly 1 5 10 15	
Ser Leu Arg Leu Ser Cys Val Ala Ser Glu Ser Ser Phe Ser Asn Asn 20 25 30	
His Met Gly Trp Tyr Arg Arg Ala Pro Gly Asn Gln Arg Glu Leu Val 35 40 45	
Ala Thr Ile Ser Pro Gly Gly Ser Thr His Tyr Val Asp Ser Val Lys 50 55 60	
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu 65 70 75 80	
Gln Met Asp Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95	
Ala Lys Gly Arg Gly Leu Gln Ala Met Gln Tyr Trp Gly Gln Gly Thr 100 105 110	

Leu Val Thr Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ser Ala
115 120 125

Ala Ala His His His His His His Gly Ala Ala Glu Gln Lys Leu Ile
130 135 140

Ser Glu Glu Asp Leu Asn Gly Ala Ala
145 150

<210> 6

<211> 468

<212> DNA

<213> Artificial Sequence

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (1)..(456)

<400> 6

cag gtg cag ctg cag gag tct ggg gga ggc ctg gtg cag gct ggg ggg 48
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
1 5 10 15

tct ctg aga ctc tcc tgt gta gcc tct gga aac acc ttc agt atc ata 96
Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Asn Thr Phe Ser Ile Ile
20 25 30

gct atg gcc tgg tac cgc cag gct cca ggg aag cag cgc gag gtg gtc 144
Ala Met Ala Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Val Val
35 40 45

gca agt att aat agt att ggc agc aca aat tat gca gac tcc gtg aag 192
Ala Ser Ile Asn Ser Ile Gly Ser Thr Asn Tyr Ala Asp Ser Val Lys
50 55 60

ggg cga ttc acc atc tcc aga gac aac gcc aag aac aca gtg tat ctg 240
Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
65 70 75 80

caa atg agc agc ctg aaa cct gag gac acg gcc gtc tat tac tgt gct 288
Gln Met Ser Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

gcc ggt aat ttg ctg gtt aag agg cct tac tgg ggc cag ggg acc ctg 336
Ala Gly Asn Leu Leu Val Lys Arg Pro Tyr Trp Gly Gln Gly Thr Leu
100 105 110

gtc acc gtc tcc tca gaa ccc aag aca cca aaa cca caa cca gcg gcc 384
Val Thr Val Ser Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala
115 120 125

gcc cat cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc tca 432
 Ala His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser
 130 135 140

gaa gag gat ctg aat ggg gcc gca tagtaacaat tg 468
 Glu Glu Asp Leu Asn Gly Ala Ala
 145 150

<210> 7

<211> 152

<212> PRT

<213> Artificial Sequence

<220>

<223> VHH with linker

<400> 7

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Val Ala Ser Gly Asn Thr Phe Ser Ile Ile
 20 25 30

Ala Met Ala Trp Tyr Arg Gln Ala Pro Gly Lys Gln Arg Glu Val Val
 35 40 45

Ala Ser Ile Asn Ser Ile Gly Ser Thr Asn Tyr Ala Asp Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Tyr Leu
 65 70 75 80

Gln Met Ser Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Ala Gly Asn Leu Leu Val Lys Arg Pro Tyr Trp Gly Gln Gly Thr Leu
 100 105 110

Val Thr Val Ser Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala
 115 120 125

Ala His His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser
 130 135 140

Glu Glu Asp Leu Asn Gly Ala Ala
 145 150

<210> 8

<211> 462

<212> DNA

<213> Artificial Sequence

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (1)..(450)

<400> 8

acc atg gcc cag gtg aaa ctg cag cag tct ggg gga gga ttg gtg cag 48
Thr Met Ala Gln Val Lys Leu Gln Gln Ser Gly Gly Gly Leu Val Gln

1

5

10

15

gct ggg ggc cct ctg agg ctc tcc tgt gca gcc tct gga cgc acc ttc 96

Ala Gly Gly Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe

20

25

30

agt aac tat gcc gtg ggc tgg ttc cgc cag gct cca ggg aag gag cgt 144

Ser Asn Tyr Ala Val Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg

35

40

45

gag ttt gtc gct gct att agc cgt gat ggt ggg cgc aca tac tat gcg 192

Glu Phe Val Ala Ala Ile Ser Arg Asp Gly Gly Arg Thr Tyr Tyr Ala

50

55

60

gac tcc gtg aag ggc cga ttc gcc gtc tcc aga gac tac gcc gag aac 240

Asp Ser Val Lys Gly Arg Phe Ala Val Ser Arg Asp Tyr Ala Glu Asn

65

70

75

80

acg gtg tat ctg caa atg aac agc ctg aaa cct gag gac acg gcc gtt 288

Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val

85

90

95

tat tac tgt aac aca agg gcc tac tgg ggc cag ggg acc cag gtc acc 336

Tyr Tyr Cys Asn Thr Arg Ala Tyr Trp Gly Gln Gly Thr Gln Val Thr

100

105

110

gtc tcc tca gcg cac cac agc gaa gac ccc agc tcc gcg gcc gcc cat 384

Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ala Ala Ala His

115

120

125

cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc tca gaa gag 432

His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu

130

135

140

gat ctg aat ggg gcc gca tagtaacaat tg 462

Asp Leu Asn Gly Ala Ala

145

150

<210> 9

<211> 150

<212> PRT

<213> Artificial Sequence

<220>

<223> VHH with linker

<400> 9

Thr Met Ala Gln Val Lys Leu Gln Gln Ser Gly Gly Gly Leu Val Gln
1 5 10 15

Ala Gly Gly Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
20 25 30

Ser Asn Tyr Ala Val Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg
35 40 45

Glu Phe Val Ala Ala Ile Ser Arg Asp Gly Gly Arg Thr Tyr Tyr Ala
50 55 60

Asp Ser Val Lys Gly Arg Phe Ala Val Ser Arg Asp Tyr Ala Glu Asn
65 70 75 80

Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Asn Thr Arg Ala Tyr Trp Gly Gln Gly Thr Gln Val Thr
100 105 110

Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ser Ala Ala Ala His
115 120 125

His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
130 135 140

Asp Leu Asn Gly Ala Ala
145 150

<210> 10

<211> 471

<212> DNA

<213> Artificial Sequence

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (1)..(459)

<400> 10

[illegible]

<210> 11

<211> 153

<212> PRT

<213> Artificial Sequence

 $\langle 220 \rangle$

<223> VHH with linker

<400> 11

Thr Met Ala Gln Val Lys Leu Gln Gln Ser Gly Gly Gly Leu Val Gln
1 5 10 15

Ala Gly Gly Pro Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Thr Phe
20 25 30

Ser Asn Tyr Ala Val Gly Trp Phe Arg Gln Ala Pro Gly Lys Glu Arg
 35 40 45
 Glu Phe Val Ala Ala Ile Ser Arg Asp Gly Gly Arg Thr Tyr Tyr Ala
 50 55 60
 Asp Ser Val Lys Gly Arg Phe Ala Val Ser Arg Asp Tyr Ala Glu Asn
 65 70 75 80
 Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val
 85 90 95
 Tyr Tyr Cys Asn Thr Arg Ala Tyr Trp Gly Gln Gly Thr Gln Val Thr
 100 105 110
 Val Ser Ser Ala His His Ser Glu Asp Pro Ser Ser Ala Ala His
 115 120 125
 His His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
 130 135 140
 Asp Leu Asn Ser Glu Lys Asp Glu Leu
 145 150

<210> 12

<211> 38

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 12

agctgcgatac gcaagcttgg taccgggaat tctctaga

38

<210> 13

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 13

aatttctaga gaattcccg taccgaagctt gcttgcgatac gc

42

<210> 14

09737476-080301
T0000-9447460

<211> 31
<212> DNA
<213> Artificial Sequence
<220>
<223> synthetic insert
<400> 14
tcgacccatg gcccgctagc caattggagc t

31

<210> 15
<211> 23
<212> DNA
<213> Artificial Sequence
<220>
<223> synthetic insert
<400> 15
ccaattggct agcgggccat ggg

23

<210> 16
<211> 22
<212> DNA
<213> Artificial Sequence
<220>
<223> primer
<400> 16
ccacccacga gggaacatcg tg

22

<210> 17
<211> 39
<212> DNA
<213> Artificial Sequence
<220>
<223> primer

<400> 17
gaattcccat ggtttacact cgaggtcttc tccaaatga 39

<210> 18

<211> 189

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR product

<400> 18
ccacccaaga gggaaacatcg tggaaaaaga agacgttcca accacgtctt caaagcaagt 60
ggattgatgt gatatctcca ctgacgtaag ggatgacgca caatccact atccttcgca 120
agacccttcc tttatataag gaagttcatt tcatttggag aggaacctga gtgtaaacca 180
tggaattc 189

<210> 19

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> sequencing primer

<400> 19
ccggcaacag gattcaatct t 21

<210> 20

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 20
agtcacatgg gatttgttct ctttcacaa ttgccttcac 40

<220>
 <223> synthetic insert
 <400> 24
 gtgtagagac aagaagaaat gaaggcaatt gtgaaaagag aacaaatccc atgg 54

 <210> 25
 <211> 24
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> synthetic insert
 <400> 25
 ggaaacagct atgaccatga ttac 24

 <210> 26
 <211> 20
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> synthetic insert
 <400> 26
 tttcccagtc acgacgttgt 20

 <210> 27
 <211> 107
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> synthetic fragment encoding PRIa leader
 <220>
 <221> CDS
 <222> (3)..(104)

<400> 27

cc atg gga ttt gtt ctc ttt tca caa ttg cct tca ttt ctt ctt gtc 47
Met Gly Phe Val Leu Phe Ser Gln Leu Pro Ser Phe Leu Leu Val
1 5 10 15

tct aca ctt ctc tta ttc cta gta ata tcc cac tct tgc cgt gcc cag 95
Ser Thr Leu Leu Leu Phe Leu Val Ile Ser His Ser Cys Arg Ala Gln
20 25 30

gtg cag ctg cag 107
Val Gln Leu

<210> 28

<211> 34

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic fragment encoding PRIa leader

<400> 28

Met Gly Phe Val Leu Phe Ser Gln Leu Pro Ser Phe Leu Leu Val Ser
1 5 10 15

Thr Leu Leu Leu Phe Leu Val Ile Ser His Ser Cys Arg Ala Gln Val
20 25 30

Gln Leu

<210> 29

<211> 21

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 29

gacatcccat ggcaagcatc a 21

<210> 30

<211> 21

aattaaccct cactaaagg

19

<210> 34

<211> 254

<212> DNA

<213> Artificial Sequence

<220>

<223> GBSS leader

<220>

<221> CDS

<222> (3)..(254)

<400> 34

cc atg gca agc atc aca gct tca cac cac ttt gtg tca aga agc caa 47
Met Ala Ser Ile Thr Ala Ser His His Phe Val Ser Arg Ser Gln
1 5 10 15

act tca cta gac acc aaa tca acc ttg tca cag ata gga ctc agg aac 95
Thr Ser Leu Asp Thr Lys Ser Thr Leu Ser Gln Ile Gly Leu Arg Asn
20 25 30

cat act ctg act cac aat ggt tta agg gct gtt aac aaa ctt gat ggg 143
His Thr Leu Thr His Asn Gly Leu Arg Ala Val Asn Lys Leu Asp Gly
35 40 45

ctc caa tca aga act aat act aag gta aca ccc aag atg gca tcc aga 191
Leu Gln Ser Arg Thr Asn Thr Lys Val Thr Pro Lys Met Ala Ser Arg
50 55 60

act gag acc aag aga cct gga tgc tca gct acc att gtt tgt gga aaa 239
Thr Glu Thr Lys Arg Pro Gly Cys Ser Ala Thr Ile Val Cys Gly Lys
65 70 75

cag gtg cag ctg cag 254
Gln Val Gln Leu Gln
80

<210> 35

<211> 84

<212> PRT

<220>

<223> GBSS leader

<213> Artificial Sequence

<400> 35

Met Ala Ser Ile Thr Ala Ser His His Phe Val Ser Arg Ser Gln Thr
 1 5 10 15
 Ser Leu Asp Thr Lys Ser Thr Leu Ser Gln Ile Gly Leu Arg Asn His
 20 25 30
 Thr Leu Thr His Asn Gly Leu Arg Ala Val Asn Lys Leu Asp Gly Leu
 35 40 45
 Gln Ser Arg Thr Asn Thr Lys Val Thr Pro Lys Met Ala Ser Arg Thr
 50 55 60
 Glu Thr Lys Arg Pro Gly Cys Ser Ala Thr Ile Val Cys Gly Lys Gln
 65 70 75 80
 Val Gln Leu Gln

<210> 36

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 36

catgcaggtg cagctgca

18

<210> 37

<211> 10

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 37

gctgcacctg

10

<210> 38

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 38

cgcaagaccc ttctctata taag

24

<210> 39

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 39

gagctcgaaat tcttattata gctcatcttt ctctgaattc agatcctctt ctgagatgag

60

<210> 40

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> linker

<400> 40

Thr Val Thr Val Ser Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

Gly Gly Gly Gly Ser Asp Ile Glu Leu Thr
20 25

<210> 41

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 41

atcctcaact tccaatcaga

20

<210> 42

<211> 19

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 42

ttcttgagag atagcttga

19

<210> 43

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 43

gatcccatgg cccgctagcc aattggagct

30

<210> 44

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 44

ccaattggct agcgggcat gg

22

<210> 45

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 45

gatccacctc gagtgtaaac catggcccg

29

<210> 46

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic insert

<400> 46

ctagcggggc atggtttaca ctcgaggtg

29

<210> 47

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 47

attgcctacg gcagccgctg

20

<210> 48

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 48

tccaaccaat tgttactatg cggcccoatt cagatcctct tctgagatga g

51

<210> 49
 <211> 25
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> sequencing primer
 <400> 49
 gtctgtctaa agtaaagtag atgcg 25

<210> 50
 <211> 60
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> PCR primer
 <400> 50
 tccaaccaat tgttatcata gctcatcttt ctactatctc agatctcttt ctgagatgag 60

<210> 51
 <211> 29
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> PCR primer
 <400> 51
 agtcccccat ggtacgtcct gtagaaacc 29

<210> 52
 <211> 25
 <212> DNA
 <213> Artificial Sequence

<220>

<223> PCR primer

<400> 52

cgttttcgtc ggtaatcacc attcc 25

<210> 53

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> sequencing primer

<400> 53

cgcaagaccc ttcctttata taag 24

<210> 54

<211> 1154

<212> DNA

<213> Artificial Sequence

<220>

<223> HCV33-hinge-CH2-CH3

<220>

<221> CDS

<222> (3)..(1136)

<400> 54

cc atg gag gtg cag ctg cag gag tca ggg gga gga ttg gtg cag gct 47
Met Glu Val Gln Leu Gln Glu Ser Gly Gly Leu Val Gln Ala
1 5 10 15

ggg ggc tct ctg aga ctc tcc tgt gca gcc tcg gga cgc gcc acc agt 95
Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser
20 25 30

ggt cat ggt cac tat ggt atg ggc tgg ttc cgc cag gtt cca ggg aag 143
Gly His Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys
35 40 45

gag cgt gag ttt gtc gca gct att agg tgg agt ggt aaa gag aca tgg 191
Glu Arg Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp
50 55 60

tat aaa gac tcc gtg aag ggc cga ttc acc atc tcc aga gat aac gcc Tyr Lys Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala 65 70 75	239
aag act acg gtt tat ctg caa atg aac agc ctg aaa cct gaa gat acg Lys Thr Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr 80 85 90 95	287
gcc gtt tat tat tgt gcc gct cga cgg gtc cgc gtg gat gat att tcc Ala Val Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser 100 105 110	335
ctg ccg gtt ggg ttt gac tac tgg ggc cag ggg acc cag gtc acc gtc Leu Pro Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val 115 120 125	383
tcc tca gaa ccc aag aca cca aaa cca caa cca caa cca cca cca Ser Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Gln Pro Gln Pro Gln 130 135 140	431
cca caa ccc aat cct aca aca gaa tcc aag tgt ccc aaa tgt cca gcc Pro Gln Pro Asn Pro Thr Thr Glu Ser Lys Cys Pro Lys Cys Pro Ala 145 150 155	479
cct gag ctg ctg gga ggg ccc tca gtc ttc atc ttc ccc ccg aaa ccc Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro 160 165 170 175	527
aag gac gtc ctg tcc att tct ggg agg ccc gag gtc acg tgc gtt gtg Lys Asp Val Leu Ser Ile Ser Gly Arg Pro Glu Val Thr Cys Val Val 180 185 190	575
gta gac gtg ggc cag gaa gac ccc gag gtc agt ttc aac tgg tac att Val Asp Val Gly Gln Glu Asp Pro Glu Val Ser Phe Asn Trp Tyr Ile 195 200 205	623
gat ggc gca gag gtg cga acg gcc aac acg agg cca aaa gag gaa cag Asp Gly Ala Glu Val Arg Thr Ala Asn Thr Arg Pro Lys Glu Glu Gln 210 215 220	671
ttc aac agc acg tac cgc gtg gtc agc gtc ctg ccc atc cag cac cag Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln 225 230 235	719
gac tgg ctg acg ggg aaa gag ttc aaa tgc aag gtc aac aac aaa gct Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala 240 245 250 255	767
ctc ccg gcc ccc atc gag aag acc atc tcc aag gcc aaa ggg cag acc Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Thr 260 265 270	815
cgg gag ccg cag gtg tac gcc ctg gcc cca cac cgg gaa gag ctg gcc Arg Glu Pro Gln Val Tyr Ala Leu Ala Pro His Arg Glu Glu Leu Ala 275 280 285	863
aag gac acc gtg agc gta acc tgc ctg gtc aaa ggc ttc tac cca cct Lys Asp Thr Val Ser Val Thr Cys Leu Val Lys Gly Phe Tyr Pro Pro 290 295 300	911

gat atc aac gtt gag tgg cag agg aac ggt cag ccg gag tca gag ggc 959
 Asp Ile Asn Val Glu Trp Gln Arg Asn Gly Gln Pro Glu Ser Glu Gly
 305 310 315

acc tac gcc acc acg cca ccc cag ctg gac aac gac ggg acc tac ttc 1007
 Thr Tyr Ala Thr Thr Pro Gln Leu Asp Asn Asp Gly Thr Tyr Phe
 320 325 330 335

ctc tac agc aag ctc tcg gtg gga aag aac acg tgg cag ccg gga gaa 1055
 Leu Tyr Ser Lys Leu Ser Val Gly Lys Asn Thr Trp Gln Arg Gly Glu
 340 345 350

acc ttc acc tgt gtg gtg atg cac gag gcc ctg cac aac cac tac acc 1103
 Thr Phe Thr Cys Val Val Met His Glu Ala Leu His Asn His Tyr Thr
 355 360 365

cag aaa tcc atc acc cag tct tcg ggt aaa taa taagaattcg agctcgaa 1154
 Gln Lys Ser Ile Thr Gln Ser Ser Gly Lys
 370 375

<210> 55

<211> 377

<212> PRT

<213> Artificial Sequence

<220>

<223> HCV33-hinge-CH2-CH3

<400> 55

Met Glu Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly
 1 5 10 15

Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser Gly
 20 25 30

His Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys Glu
 35 40 45

Arg Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp Tyr
 50 55 60

Lys Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys
 65 70 75 80

Thr Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala
 85 90 95

Val Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser Leu
 100 105 110

Pro Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser
 115 120 125

Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Gln Pro Gln Pro Gln Pro
 130 135 140
 Gln Pro Asn Pro Thr Thr Glu Ser Lys Cys Pro Lys Cys Pro Ala Pro
 145 150 155 160
 Glu Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
 165 170 175
 Asp Val Leu Ser Ile Ser Gly Arg Pro Glu Val Thr Cys Val Val Val
 180 185 190
 Asp Val Gly Gln Glu Asp Pro Glu Val Ser Phe Asn Trp Tyr Ile Asp
 195 200 205
 Gly Ala Glu Val Arg Thr Ala Asn Thr Arg Pro Lys Glu Glu Gln Phe
 210 215 220
 Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp
 225 230 235 240
 Trp Leu Thr Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu
 245 250 255
 Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Thr Arg
 260 265 270
 Glu Pro Gln Val Tyr Ala Leu Ala Pro His Arg Glu Glu Leu Ala Lys
 275 280 285
 Asp Thr Val Ser Val Thr Cys Leu Val Lys Gly Phe Tyr Pro Pro Asp
 290 295 300
 Ile Asn Val Glu Trp Gln Arg Asn Gly Gln Pro Glu Ser Glu Gly Thr
 305 310 315 320
 Tyr Ala Thr Thr Pro Pro Gln Leu Asp Asn Asp Gly Thr Tyr Phe Leu
 325 330 335
 Tyr Ser Lys Leu Ser Val Gly Lys Asn Thr Trp Gln Arg Gly Glu Thr
 340 345 350
 Phe Thr Cys Val Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
 355 360 365
 Lys Ser Ile Thr Gln Ser Ser Gly Lys
 370 375

<210> 56

<211> 1172

<212> DNA

<213> Artificial Sequence

<220>

<223> hinge-HCV33-CH2-CH3-SEKDEL

<220>

<221> CDS

<222> (3)..(1154)

<400> 56

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   Met Glu Val Gln Leu Gln Glu Ser Gly Gly Leu Val Gln Ala
     1             5             10             15

ggg ggc tct ctg aga ctc tcc tgt gca gcc tcg gga cgc gcc acc agt      95
Gly Gly Ser Leu Arg Leu Ser Cys Ala Ser Gly Arg Ala Thr Ser
                20             25             30

ggt cat ggt cac tat ggt atg ggc tgg ttc cgc cag gtt cca ggg aag      143
Gly His Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys
                35             40             45

gag cgt gag ttt gtc gca gct att agg tgg agt ggt aaa gag aca tgg      191
Glu Arg Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp
                50             55             60

tat aaa gac tcc gtg aag ggc cga ttc acc atc tcc aga gat aac gcc      239
Tyr Lys Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala
                65             70             75

aag act acg gtt tat ctg caa atg aac agc ctg aaa cct gaa gat acg      287
Lys Thr Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr
                80             85             90             95

gcc gtt tat tat tgt gcc gct cga ccg gtc cgc gtg gat gat att tcc      335
Ala Val Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser
                100            105            110

ctg ccg gtt ggg ttt gac tac tgg ggc cag ggg acc cag gtc acc gtc      383
Leu Pro Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val
                115            120            125

tcc tca gaa ccc aag aca cca aaa cca caa cca caa cca caa cca caa      431
Ser Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Gln Pro Gln Pro Gln
                130            135            140

cca caa ccc aat cct aca aca gaa tcc aag tgt ccc aaa tgt cca gcc      479
Pro Gln Pro Asn Pro Thr Thr Glu Ser Lys Cys Pro Lys Cys Pro Ala
                145            150            155

cct gag ctc ctg gga ggg ccc tca gtc ttc atc ttc ccc ccg aaa ccc      527
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro
                160            165            170            175

aag gac gtc ctc tcc att tct ggg agg ccc gag gtc acg tgc gtt gtg      575
Lys Asp Val Leu Ser Ile Ser Gly Arg Pro Glu Val Thr Cys Val Val
                180            185            190

gta gac gtg ggc cag gaa gac ccc gag gtc agt ttc aac tgg tac att      623
Val Asp Val Gly Gln Glu Asp Pro Glu Val Ser Phe Asn Trp Tyr Ile
                195            200            205
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gat ggc gca gag gtg cga acg gcc aac acg agg cca aaa gag gaa cag Asp Gly Ala Glu Val Arg Thr Ala Asn Thr Arg Pro Lys Glu Glu Gln 210 215 220	671
ttc aac agc acg tac cgc gtg gtc agc gtc ctg ccc atc cag cac cag Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln 225 230 235	719
gac tgg ctg acg ggg aaa gag ttc aaa tgc aag gtc aac aac aaa gct Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala 240 245 250 255	767
ctc ccg gcc ccc atc gag aag acc atc tcc aag gcc aaa ggg cag acc Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Thr 260 265 270	815
cgg gag ccg cag gtg tac gcc ctg gcc cca cac cgg gaa gag ctg gcc Arg Glu Pro Gln Val Tyr Ala Leu Ala Pro His Arg Glu Glu Leu Ala 275 280 285	863
aag gac acc gtg agc gta acc tgc ctg gtc aaa ggc ttc tac cca cct Lys Asp Thr Val Ser Val Thr Cys Leu Val Lys Gly Phe Tyr Pro Pro 290 295 300	911
gat atc aac gtt gag tgg cag agg aac ggt cag ccg gag tca gag ggc Asp Ile Asn Val Glu Trp Gln Arg Asn Gly Gln Pro Glu Ser Glu Gly 305 310 315	959
acc tac gcc acc acg cca ccc cag ctg gac aac gac ggg acc tac ttc Thr Tyr Ala Thr Thr Pro Gln Leu Asp Asn Asp Gly Thr Tyr Phe 320 325 330 335	1007
ctc tac agc aag ctc tcg gtg gga aag aac acg tgg cag cgg gga gaa Leu Tyr Ser Lys Leu Ser Val Gly Lys Asn Thr Trp Gln Arg Gly Glu 340 345 350	1055
acc ttc acc tgt gtg gtg atg cac gag gcc ctg cac aac cac tac acc Thr Phe Thr Cys Val Val Met His Glu Ala Leu His Asn His Tyr Thr 355 360 365	1103
cag aaa tcc atc acc cag tct tcg ggt aaa tct gag aaa gat gag cta Gln Lys Ser Ile Thr Gln Ser Ser Gly Lys Ser Glu Lys Asp Glu Leu 370 375 380	1151
taa taagaattcg agctcgaa	1172
<210> 57	
<211> 383	
<212> PRT	
<213> Artificial Sequence	
<220>	
<223> hinge-HCV33-CH2-CH3-SEKDEL	
<400> 57	

Met Glu Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala Gly
 1 5 10 15
 Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Arg Ala Thr Ser Gly
 20 25 30
 His Gly His Tyr Gly Met Gly Trp Phe Arg Gln Val Pro Gly Lys Glu
 35 40 45
 Arg Glu Phe Val Ala Ala Ile Arg Trp Ser Gly Lys Glu Thr Trp Tyr
 50 55 60
 Lys Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys
 65 70 75 80
 Thr Thr Val Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala
 85 90 95
 Val Tyr Tyr Cys Ala Ala Arg Pro Val Arg Val Asp Asp Ile Ser Leu
 100 105 110
 Pro Val Gly Phe Asp Tyr Trp Gly Gln Gly Thr Gln Val Thr Val Ser
 115 120 125
 Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Gln Pro Gln Pro Gln Pro
 130 135 140
 Gln Pro Asn Pro Thr Thr Glu Ser Lys Cys Pro Lys Cys Pro Ala Pro
 145 150 155 160
 Glu Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
 165 170 175
 Asp Val Leu Ser Ile Ser Gly Arg Pro Glu Val Thr Cys Val Val Val
 180 185 190
 Asp Val Gly Gln Glu Asp Pro Glu Val Ser Phe Asn Trp Tyr Ile Asp
 195 200 205
 Gly Ala Glu Val Arg Thr Ala Asn Thr Arg Pro Lys Glu Glu Gln Phe
 210 215 220
 Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp
 225 230 235 240
 Trp Leu Thr Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu
 245 250 255
 Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Thr Arg
 260 265 270
 Glu Pro Gln Val Tyr Ala Leu Ala Pro His Arg Glu Glu Leu Ala Lys
 275 280 285
 Asp Thr Val Ser Val Thr Cys Leu Val Lys Gly Phe Tyr Pro Pro Asp
 290 295 300
 Ile Asn Val Glu Trp Gln Arg Asn Gly Gln Pro Glu Ser Glu Gly Thr
 305 310 315 320

Tyr Ala Thr Thr Pro Pro Gln Leu Asp Asn Asp Gly Thr Tyr Phe Leu
325 330

Tyr Ser Lys Leu Ser Val Gly Lys Asn Thr Trp Gln Arg Gly Glu Thr
340 345 350

Phe Thr Cys Val Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
355 360 365

Lys Ser Ile Thr Gln Ser Ser Gly Lys Ser Glu Lys Asp Glu Leu
370 375 380

<210> 58

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 58

aggggaccca ggtaaccgtc tctcagaac c

31

<210> 59

<211> 37

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 59

gagctttgtt gttgaccttg catttgaact ctttccc

37

<210> 60

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 60

caaatgcaag gtcaacaaca aagctc

26

<210> 61

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 61

ttcgagctcg aattcttatt atttaccga agactgggtg at

42

<210> 62

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> sequencing primer

<400> 62

ctgaggagac ggtgacctgg gtcacct

27

<210> 63

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 63

agccccctgag ctctctgggag ggcctcagt ctcatcttc cccocg

46

<210> 64

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 64

ttcgagctcg aattottatt atttaccoga agactgggtg atggatttct ggggttagtg 60
g 61

<210> 65

<211> 79

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 65

ttcgagctcg aattottatt atagctcato ttctcagat ttaccogaag actgggtgat 60
ggatttctgg gtgtagtgg 79

<210> 66

<211> 461

<212> DNA

<213> Artificial Sequence

<220>

<223> VHH with linker

<220>

<221> CDS

<222> (3)..(449)

<400> 66

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Met Ala Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln
1 5 10 15
gct ggg ggg tct ctg agg ctc tcc tgt gca gcc tct gga agc att ttc 95
Ala Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Ile Phe
20 25 30

aga cgt ccg cat atg ggt tgg ttc cgc cag gct cca ggg cag gag cgc 143
 Arg Arg Pro His Met Gly Trp Phe Arg Gln Ala Pro Gly Gln Glu Arg
 35 40 45

gag ttg gtc gca ctg att tct gcg ggt ggt cgt aca tgg tat gca gac 191
 Glu Leu Val Ala Leu Ile Ser Ala Gly Gly Arg Thr Trp Tyr Ala Asp
 50 55 60

tcc gtg aag ggc cga ttc acc atc tcc aga gac aac gcc aag aac acg 239
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr
 65 70 75

ctg tat ctg caa atg aac agc ctg aaa cct gag gac acg gcc gtt tat 287
 Leu Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr
 80 85 90 95

tac tgt act gcc ggg ggt tgc tac tgg ggc cag ggg acc cag gtc acc 335
 Tyr Cys Thr Ala Gly Gly Ser Tyr Trp Gly Gln Gly Thr Gln Val Thr
 100 105 110

gtc gcc tca gaa ccc aag aca cca aaa cca caa cca gcg gcc gcc cat 383
 Val Ala Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala Ala His
 115 120 125

cac cat cac cat cac ggg gcc gca gaa caa aaa ctc atc tca gaa gag 431
 His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu
 130 135 140

gat ctg aat ggg gcc gca tagtaacaat tg 461
 Asp Leu Asn Gly Ala Ala
 145

<210> 67

<211> 149

<212> PRT

<213> Artificial Sequence

<220>

<223> VHH with linker

<400> 67

Met Ala Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Leu Val Gln Ala
 1 5 10 15

Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ser Ile Phe Arg
 20 25 30

Arg Pro His Met Gly Trp Phe Arg Gln Ala Pro Gly Gln Glu Arg Glu
 35 40 45

Leu Val Ala Leu Ile Ser Ala Gly Gly Arg Thr Trp Tyr Ala Asp Ser
 50 55 60

Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu
 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Lys Pro Glu Asp Thr Ala Val Tyr Tyr
 85 90 95
 Cys Thr Ala Gly Gly Ser Tyr Trp Gly Gln Gly Thr Gln Val Thr Val
 100 105 110
 Ala Ser Glu Pro Lys Thr Pro Lys Pro Gln Pro Ala Ala Ala His His
 115 120 125
 His His His His Gly Ala Ala Glu Gln Lys Leu Ile Ser Glu Glu Asp
 130 135 140
 Leu Asn Gly Ala Ala
 145

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